Discovery of previously unknown immunodeficiency

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Severe autoimmunity in childhood can be an indication of a primary immunodeficiency (PID) – this has now been demonstrated in a 13-year-old patient by a research group from the MedUni Vienna belonging to the CeMM Research Center for Molecular Medicine of the AAS and the St. Anna paediatric hospital. A previously unknown B-cell defect was

identified in the teenager with the aid of so-called "next generation sequencing", with which genetic mutations in the genetic material can be detected within a few days. The study has been published in the leading journal *Blood*.

"Our discovery created a sense of relief in the family as they now know at last what is wrong with the boy," says Kaan Boztug, who works routinely as a doctor at the University Department of Paediatrics and Adolescent Medicine treating seriously ill children, and as a researcher at CeMM, searching for the molecular causes of diseases of the immune system using the most modern genetic technologies. In this specific case a defect in the PRKCD gene was discovered. This causes a malfunction in the regulation of the B lymphocytes which are regarded as "antibody factories". Severe autoimmunity develops as a consequence.

According to Boztug and Elisabeth Förster-Waldl, paediatrician and immunologist at the University Department of Paediatrics and Adolescent Medicine of the MedUni Vienna, not only diagnostic, but also therapeutic, consequences can be derived from the recently successful molecular identification of the deficiency. From early childhood the patient had suffered periodically from severe autoimmunity of the kidneys, lymph nodes and connective tissues. The now 13-year-old had previously been globally immunosuppressed with cortisone for long periods but now the target of the therapy can be precisely isolated. Says Förster-Waldl: "Only when you know the mechanism, an individually-tailored therapy can be appropriately used or developed."

Data from the Anglo-American world assume that the prevalence of a clinically relevant immunodeficiency that can sometimes involve life-threatening consequences for those affected lies at between 1:1200 and 1:2000. Such figures can only be estimated for Austria as the systematic collection of data has only been taking place for the last two years.

At present around 30 to 40 percent of these deficiencies remain without a precise diagnosis according to Förster-Waldl. This could now change with the aid of the latest diagnostic processes including "next generation sequencing". Most immunodeficiencies are classified as so-called "rare diseases". Kaan Boztug: "However, the sum total of all these defects cannot be categorised as rare."

More information: Salzer, E. et al. B cell deficiency and severe autoimmunity caused by deficiency of protein kinase C delta, *Blood*. doi. 10.1182/blood-2012-10-460741

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